REMARKS

Claims 1-5, 14-16, 19, and 24-26 have been cancelled, without prejudice, and new claims 28-75 have been added. Applicant reserves the right to pursue the subject matter of the canceled claims in this or continuing applications. Applicant and Applicant's attorneys thank Examiners Yu and Caputa for the time and courtesies extended by the Examiners during the Examiner Interview of February 26, 2003.

Claim Rejections – 35 U.S.C. § 112

Claims 1-5, 14-16, 19 and 24-26 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. The office action states that claims 2, 14, and 25-26 recite the term "agent" without an antecedent basis. New claims 28-55 do not use the term "agent." Therefore, the rejection under 35 U.S.C. § 112, second paragraph, is overcome and should be withdrawn.

Claim Rejections – 35 U.S.C. § 102

Claims 1-5, 14-16, 19 and 24-26 stand rejected under 35 U.S.C. § 102 as being anticipated by Shoyab, et al. Applicant respectfully traverses this rejection.

Several breakthrough discoveries by the Applicant provide the foundation of the claimed invention. Contrary to teachings of Shoyab et al., the Applicant discovered that GP88, the full length 88KDa precursor (encoded by SEQ ID 16), is a highly active and tumorigenic molecule. The Applicant was the first to show that the protein encoded by SEQ ID 16 is stringently required for the proliferation of tumor cells. The Applicant was first to show that inhibition of the protein encoded by SEQ ID 16 results in inhibition of tumorigenic properties. The Applicant was also the first to show that the protein encoded by SEQ ID 16 is overexpressed in tumor cells and tightly regulated in normal cells. Furthermore, the Applicant was the first to show that the protein encoded by SEQ ID 16 is tumorigenic (i.e., GP88 confers on a cell the ability to cause a tumor when injected into an

animal). See, e.g. Specification at 3, 17, 56, 62 and Figure 3. Thus, the instant application provides for the first time the knowledge that the full length precursor (GP88) is an active, stringently-required, overexpressed, and highly tumorigenic growth factor for tumor cells, and that antibodies to the full length precursor (GP88) significantly inhibit the proliferation of tumor cells.

Shoyab et al. teach that the epithelin precursor encoded by SEQ ID NO. 16 (GP88) is inactive. According to Shoyab et al., "[t]he unprocessed epithelin precursor has no activity in any of these assays[1]. Shoyab et al. ('510) at page 52, lines 13-18. Shoyab et al. were unable to confirm any activity of the unprocessed epithelin precursor (i.e., GP88). There is no disclosure or motivation based on Shoyab et al. to make an antibody directed to an inactive precursor. Shoyab et al.'s entire disclosure is directed to the processed 6KDa epithelins, the only biologically "active" molecules recognized by Shoyab et al.

Applicant's claims are directed to antibodies to epitopes of the precursor protein which is encoded by SEQ ID 16, wherein the antibody has anti-tumorigenic activity. New claim 28 recites a:

> composition comprising an isolated antibody capable of binding to an epitope of the protein encoded by SEQ ID NO. 16, wherein said antibody has anti-tumorigenic activity.

Shoyab et al. do not disclose or suggest any antibodies to the precursor protein or any antibodies having anti-tumorigenic activity. The antibodies discussed in Shoyab et al. are raised against the processed 6KDa epithelin peptides.

[1] The "assays" referred to by Shoyab et al. include assays for determining the biological effects of epithelins (e.g., the inhibitory effect of epithelin 1 on A431 cells, and mitogenic effect on normal cell lines). See Shoyab et al. '510 at page 52, lines 5-18.

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If Examiner Yu should believe that anything further may be required to place this application in even better form for allowance, she is cordially invited to telephone the undersigned attorneys for Applicant.

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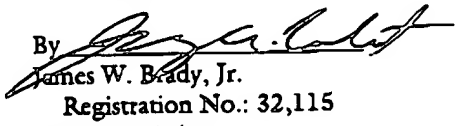
Respectfully submitted,

By 

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Moreover, Shoyab et al. teach that the processed 6KDa epithelins are anti-tumorigenic proteins. Antibodies directed to epithelins would therefore be expected to inhibit the anti-tumorigenic function of epithelins, resulting in increased rather than decreased tumor cell growth. According to Shoyab et al.:

> notwithstanding their functional differences, both epithelin 1 and epithelin 2 may be useful as anti-tumor agents since they both demonstrate the ability to inhibit the growth of neoplastic cells, although applicants' initial data suggests that epithelin 1 may be a more powerful and/or effective tumor inhibitor. [Shoyab, '510 at page 27, lines 22-27][emphasis added].

Shoyab et al. further state that "[e]pithelins and related derivatives, analogues, and peptides thereof may be used along or with at least one other anti-proliferative compound, including, for example, an interferon, TFG-β (sic), tumor necrosis factors, etc. in the treatment of neoplastic and other growth related diseases. Carcinomas may also be treated by inducing production of epithelins in the carcinoma cells." Shoyab, '510 at page 28, lines 17-22 (emphasis added). Therefore, according to Shoyab, epithelins are anti-proliferative compounds useful in the treatment of tumors. In contrast, Applicant was the first to teach that the full length 88KDa precursor (GP88) encoded by SEQ ID NO: 16 causes and promotes the growth of tumors.

In summary, Applicant's claims are directed to compositions and methods comprising an antibody capable of binding to an epitope of the protein encoded by SEQ ID NO. 16, wherein the antibody has anti-tumorigenic activity, while Shoyab et al. refer only to anti-epithelen antibodies. Shoyab at al. do not disclose any anti-tumorigenic antibodies capable of binding to any epitope of the protein encoded by SEQ ID NO. 16. Thus, Shoyab et al. fail to disclose or suggest Applicant's claimed invention. The rejection under 35 U.S.C. § 102 should therefore be withdrawn in view of the claims as amended, each of which requires an anti-tumorigenic antibody.